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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,631	08/31/2001	Michael E. Rickey	00166.112-US00	8160

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EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,631	RICKEY ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *08312001+* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

The information disclosure statements filed August 31, 2001, October 26, 2001 and February 3, 2003 have been considered. Please see the attached initialed PTO-1449s.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-30, 32-50, 52, 54-60, 63-69 and 71-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. in view of Tice et al. ('330), Hodgman et al., Ed., Gutsell, Jr. et al. and Tracy et al.

Lewis et al. teach manufacture of microparticles by dissolving a polymeric material such as polylactide, polylactide-co-glycolide or polyglycolide (see page 7, fourth paragraph) in an organic solvent such as methylene chloride (see page 8, first full paragraph), adding the material to be microencapsulated as an aqueous solution to form a water-in-oil emulsion, adding a non-solvent for the polymer such as silicone oil (see page 8, second paragraph), clearly as a coacervating agent, and then quenching with a second non-solvent for the polymer such as heptane (see page 10, second paragraph). In the first few lines of page 6 they discuss the residual solvent level and a method to reduce the methylene chloride level to 0.1% or less by vacuum extraction. On page 14 first full paragraph, Lewis et al. teach luteinizing hormone releasing hormone analog (LHRH) as a desirable material to be microencapsulated.

Lewis et al. do not teach washing the microcapsules as a final step and, therefore, do not teach washing with ethanol or a blend of ethanol and heptane to reduce the level of residual halogenated solvent.

Tice et al. ('330) teach a method of making microcapsules similar to that taught by Lewis et al. They teach methylene chloride as the solvent for dissolving the active ingredient at column 2, line 58, the same preferred group of polymeric wall forming materials at column 3, lines 29-33, and quenching in water or an organic liquid at column 3, lines 41-44. They discuss removal of residual solvent at column 4, lines 33-40. They state, "the remainder of the solvent in the microcapsules is removed by extraction. In this second step, the microcapsules can be suspended in the same continuous phase processing medium used in step one . . . or in another liquid. The extraction medium extracts the solvent from the mirocapsules *(sic)* and yet does not dissolve the microcapsules." In their examples the active ingredient is progesterone microencapsulate in poly(DL-lactide) using methylene chloride as the first solvent and aqueous poly(vinyl alcohol) as the quenching phase. Therefore, according to their teachings, they use deionized water as the washing solvent. At column 6, lines 59-61 they state, "[T]his washing step extracted residual methylene chloride remaining in the microcapsules and hardened the microcapsules."

Hodgman et al., Eds. teach that alcohol is a good solvent for methylene chloride. The footnotes to the table explain that "alcohol" means ethanol.

Gutsell, Jr. et al. teach that heptane is a solvent for methylene chloride, see column 5, lines 32-34.

Tracy et al. teach that it is conventional to use a mixture of heptane and ethanol in preparation of microparticles.

It would have been obvious to one of ordinary skill in the art to add the washing step of Tice et al. ('330) to the process of Lewis et al. in order to further reduce the level of residual methylene chloride. Said person of ordinary skill would have realized that using a better solvent for methylene chloride would result in better removal of residual solvent and would therefore be motivated to wash the microcapsules with ethanol since methylene chloride is infinitely soluble in ethanol, as taught by Hodgman et al., Eds. Similarly, it would have been obvious to one of ordinary skill in the art to use heptane for washing the microcapsules from the combined teachings of Tice et al. ('330) and Gutsell, Jr. et al. Tice et al. ('330) teach to use the same solvent for washing as was used for the quench step. If one uses heptane as the quench liquid, as taught by Lewis et al., it follows from the teaching of Tice et al. ('330) to use heptane as the wash liquid. As before, said person of ordinary skill would expect improved results by using a better solvent for methylene chloride than water for the wash solvent. Use of a mixture of heptane and ethanol is rendered obvious by Tracy et al. One of ordinary skill would expect to achieve beneficial results by using heptane/ethanol as the quench solvent as well as the wash solvent in accordance with the teachings of Tice et al. ('330). The proportions of ethanol to heptane are not seen as a critical limitation, absent convincing evidence to the contrary, and it would be well within the ordinary level of skill in the art to perform routine experimentation to arrive at desired proportions. With regard to claims 6 and 25, similarly, it is well within the ordinary level of skill in the art to select the desired temperature. The prior art shows cold solvents as well as hot solvents and the selection of a temperature is easily determinable by routine experimentation. With

regard to claims 14, 15, 29, 44, 45, 67 and 69, it would have been obvious to one of ordinary skill in the art to perform the extraction step until the level of residual solvent is at the desired level. With regard to the specific material to be microencapsulated, e.g., peptide or goserelin, it is clear from the specification and the prior art both that the choice of such material is not critical and it is considered that selection of the material would have been within the level of skill in the art to determine.

4. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. in view of Tice et al. ('330), Hodgman et al., Eds., Gutsell, Jr. et al. and Tracy et al. as applied to claims 1-30, 32-50, 52, 54-60, 63-69 and 71-87 above, and further in view of Thanoo et al.

Thanoo et al. teach that it is conventional to use a static mixer in methods of making microparticles, see column 4, lines 57-59. It would have been obvious to one of ordinary skill in the art to use a static mixer to perform the process of Lewis et al. as modified by the teachings of the other references with the expectation of obtaining beneficial results.

5. Claims 51, 53, 61, 62 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. in view of Tice et al. ('330), Hodgman et al., Eds., Gutsell, Jr. et al. and Tracy et al. as applied to claims 1-30, 32-50, 52, 54-60, 63-69 and 71-87 above, and further in view of Rickey et al. ('503).

Rickey et al. ('503) teach that preparation of microcapsules containing risperidone, 9-hydroxyrisperidone or pharmaceutically acceptable salts thereof (see column 11, line 64-column 12, line 2) wherein the preferred solvent is a mixture of ethyl acetate and benzyl alcohol (see column 16, lines 44-45) and the preferred wash solvent is ethanol (see column 16, lines 59-64). It would have been obvious to one of ordinary skill in the art to use ethyl acetate/benzyl alcohol as the solvent in the process of Lewis et al. as modified by the teachings of the other references when microencapsulating risperidone or related compound with the expectation of obtaining the benefits taught by Rickey et al. (503).

Conclusion

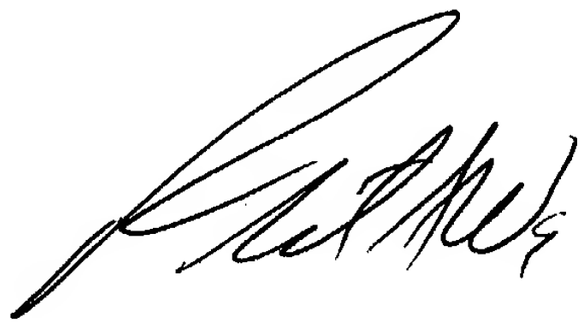
6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cohen et al. teach that if one is microencapsulating protein the best polymer to use as the wall material is poly(lactic/glycolic acid).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (703) 308-4471. The examiner can normally be reached on Monday - Friday, 9:00 - 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low can be reached on (703) 308-2923. The fax phone

number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Robert A. Wax
Primary Examiner
Art Unit 1653